Organotypic ex vivo Culture of Liver Tissue for Assessment of HCC Chemoprevention Drug

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There is no curative therapy for liver cancer, the second leading cancer mortality worldwide, therefore cancer chemoprevention is the most impactful strategy to improve the dismal prognosis. Predictors of response to chemoprevention therapy for liver cancer to identify the patients who most benefit from the therapy was completed. Fresh liver tissues from 13 patients were treated with a liver cancer chemoprevention drug RhoA, which inhibits a liver cancer driver gene RhoA identified by bioinformatics systems biology analysis, and reversal of a liver cancer risk gene signature, which was determined prior to liver culture was validated. Subsequently, clinical, histological, and/or molecular predictors for the gene signature reversal were determined. Among the 13 livers, 8 and 5 had milder (fibrosis stage F0 to F2) and severer (F3 and F4) liver fibrosis, respectively. Six patients were predicted as having high-liver cancer risk gene signature. By the drug RhoA treatment, 5 patients showed statistically significant reversal of the gene signature. High-risk gene signature before treatment and milder fibrosis stage were significantly correlated with the gene signature reversal ($p<0.05$). Pre-treatment presence of high-risk gene signature and less fibrosis stage were identified as predictors of response to drug RhoA, which will enable identification of the patients to be prioritized for liver cancer chemoprevention therapy. This approach will be widely applicable for other cancer types to realize prevention of cancer like cardio- or cerebrovascular diseases.

Awards Won:

Fourth Award of $500